REMARKS

Claims 37-47, presented hereby, are pending. Election of the invention of Group II, claims 25-34, as represented by the present claims, is confirmed.

Original claims 28-34 are replaced by claims 37-47, in accordance with the instant Amendment. Support for specifying the mycobacteria of the MTC group and the MOTT group in for claims 37-47 can be found on page 2, lines 1-5 of the PCT specification. Basis for introducing formula V can be found throughout the specification as well as in originally filed claim 18. Other changes in the claims are made to more clearly define the instant invention.

Applicants wish to thank the Examiner for permitting the shift in election, i.e., permitting the election of the subject matter in original claims 25-34.

Compliance with the sequence rules is effected by the Sequence Listing and associated papers filed, concurrently, herewith.

Rejections of record against claims 25-27 are rendered moot by the instant Amendment, whereby claims 25-27 are canceled.

Reconsideration is requested with respect to the rejection under 35 USC 112, ¶2, in view of the instant Amendment.

Claims 25-27 are cancelled. The terms "capable of" and "in particular" are not found in the instant claims.

Claims were rejected under 35 USC 103(a) based on the combined terachings of Hogan et al. (US 5,541,308) in view of Shah et al. (US 5,21,300), and further in view of Britschgi et al. (US

5,726,021) and further in view of Hyldig-Nielsen et al. (WO 93/32305). Reconsideration is requested.

The statement of rejection admits that neither Hogan et al., Shah et al., nor Britschgi teaches PNA probes in the detection of mycobacteria. It is correct that Hyldig-Nielsen et al. teach the use of PNA probes, however, for a different purpose then that of the presently claimed invention, namely for use with respect to *Neisseria gonorroeae* and *Chlamydia trachomatis*. Mycobacteria are neither taught nor suggested by Hyldig-Nielsen et al. As will appear from the following explanation, Mycobacteria differ from many other species in their physical structure.

Mycobacteria are characterised by a complex cell wall containing myolic acid, complex waxes and unique glycolipids, and accordingly mycobacteria possess an extreme resistance to chemical and physical stress as compared to other bacteria. Thus, mycobacteria are very difficult to penetrate and lyse. It is generally recognised that this cell wall of the mycobacteria prevents penetration of even short nucleic acid probes (i.e. shorter than 30 nucleic acids) unless the sample containing the mycobacteria is subjected to harsh conditions like dewaxing with xylene, enzymatic treatment, or other disruption of the cell wall, e.g., by sonication, cf. US 5,582,985 (cited in the present specification). This is, of course, an option if one is not interested in studying the morphology of the cells of the sample, since such treatments will release the target nucleic acids. Accordingly, the prior art, in effect, teaches away from the use of short probes.

Furthermore, PNAs are different from DNA and RNA probes in many respects and are not directly comparable. Thus, it cannot be generally assumed that PNA probes will work, just because

DNA and RNA probes do. Likewise, it cannot be concluded that because PNA probes are applicable in the detection of other bacteria, then PNA probes may also be successfully applied in the detection of Mycobacteria. Obviousness is not established by "the rather general urge commonly felt by alert research men to investigate each new . . . process that appears in order to see if it can be used to improve any of the processes in which they are currently interested." *Ex parte Polak*, 83 USPQ 135, 136-137 (POBdApp 1949). "Obvious to experiment" is not the standard for obviousness under §103 of the statute; "selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings." *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1532 (Fed. Cir. 1988). Moreover, where the practitioner cannot foresee the results, obviousness to try "*with a reasonable chance of success*" does not distinguish over obvious to try as an improper basis for a finding of obviousness under §103. *Ex parte Old*, 229 USPQ 196 (BPA & I 1985) (*emphasis added*).

> An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, bu the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain conditions were perused.

In re Lilly & Co., 14 USPQ2d 1741, 1743 (Fed. Cir. 1990).

Accordingly, it could not have been predicted that the PNA probes used in accordance with the presently claimed invention would have been applicable in the detection of Mycobacteria. Furthermore, it would not have been expected that the PNA probes would be able to bind to and,

thus, detect Mycobacteria given the characteristics of Mycobacteria, and even distinctly discriminate between various species of Mycobacteria, differing only by one or a few nucleobases.

Accordingly, Applicants submit that the presently claimed invention is patentable over the teachings of the cited references and, therefore, withdrawal of the rejection is in order.

Applicants wish to thank the Examiner for the indication of allowable subject matter, i.e., the subject matter of SEQ ID NOs 40, 44, 76, 89, and 90. It is respectfully submitted that, as explained above, patentability estends to the full scope of the invention as presently claimed.

It should also be taken into consideration that the presently claimed invention is, in fact, exemplified by a representative selection of PNA probes of the whole scope of the present claims, cf. the Examples. Thus, specific PNA probes targeting MTC 23S and 16S (cf. all Examples), MOTT 23S and 16S (cf. all Examples), drug resistance (cf. in particular Examples 2, 3, and12), and precursor rRNA (cf. in particular Examples 2,3 and 11) are exemplified.

Furthermore, specific PNA probes targeting MTC 23S, 16S, and 5S, MOTT 23S, and 16S, drug resistance, and precursor rRNA are envisaged in the specification. It has further been shown in the Examples that the probes are able to discriminate between the MTC group and the MOTT group (cf. all Examples), and that no cross-reactivity to non-related species (cf. in particular Example 4) as well as non-relevant Mycobacteria (i.e. those not part of the MTC and MOTT groups) is observed (cf. in particular Examples 4, 5 and 7). Also, it has been shown that mycobacteria of the MTC and the MOTT group can be detected simultaneously by applying MTC probes and MOTT probes labelled with different colours, cf. Example 10. A huge number of clinical specimens was

tested, cf. in particular Examples 6, 8 and 9, thus confirming the applicability and usefulness as well as the specificity and sensitivity of the presently claimed invention.

Favorable action is requested.

Respectfully submitted,

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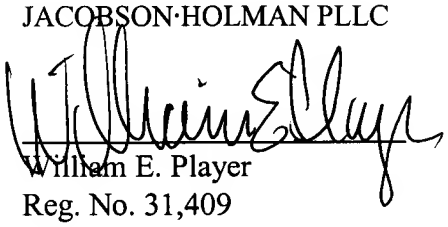
By: 

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